

Atty. Dkt. No. 072827-1905

Remarks

Applicant respectfully requests reconsideration of the present application in view the foregoing amendments and in view of the reasons that follow.

Claims 5-6 and 21-27 are currently pending in this application. Claims 25-27 are new and have been added in the instant amendment. Support for "said compound is active at a serotonin reuptake site and at a N-methyl-D-aspartate (NMDA) receptor" is provided throughout the specification, for example at page 2, lines 17-20; support for "said compound has an NMDA receptor IC<sub>50</sub> of about 50 nM to about 1  $\mu$ M" can be found at page 3, lines 9-11; and support for "said compound has an NMDA receptor IC<sub>50</sub> of about 100 nM to about 800 nM" can be found at page 3, lines 11-12. Accordingly, the amendments raise no issue of new matter.

Rejection under 35 U.S.C. § 103(a)

The rejection of claims 5-6 and 21-24 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Jones *et. al.*, (Journal of Medicinal Chemistry, 1971, 14:161-164) is respectfully traversed.

Applicant respectfully submits that none of the compounds disclosed in the Jones reference falls within the limitations of the instant claims. The examiner alleges, however, that it would be obvious for one of ordinary skill in the art to modify a compound of the Jones reference (presumably one of the compounds disclosed in Table III) to obtain a compound that meets the limitations of the claims.

In order to establish a prima facie case of obviousness, it is necessary that the prior art as a whole disclose each and every limitation of the claim, that there is a reasonable expectation of success, and that there be some motivation, either in the prior art references or in the knowledge of the person of ordinary skill in the art, to make the asserted combination or modify or combine the reference teachings (MPEP § 2142).

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To support a motivation for a skilled artisan to make such modifications to the compounds disclosed in Jones, the Examiner states that the compounds of the Jones reference are "constituted with same ingredients and share common utilities." However, the Jones reference does not teach or suggest to make any modifications to the compounds disclosed in Table III, or any advantages that any such modifications might have. Furthermore, the Jones reference teaches that three of the compounds studied in the reference (compound 6, 16 and 17) "have activities comparable with those of known clinically effective antidepressants" and three of the compounds (5, 15 and 18) are "more active [than known clinically effective antidepressants] in the pharmacological and biochemical tests reported". See page 161, right column, last full paragraph. It is notable that the activities of all of the compounds in Table III, which shows saturated compounds corresponding to "generic structure V" (see page 161, column 1), fall short of the activities of these six compounds, each of which correspond to "generic structure IV" (*i.e.* the olefinic series). Along the same lines, the Jones reference teaches that "saturated compounds are in general marginally less active..." See page 162 right column, first sentence of the last full paragraph. Therefore, if one of ordinary skill in the art was motivated to make modifications to any compounds, such motivation would be directed to the unsaturated compounds in Table I (*e.g.* compounds 5, 15 and 18) and not the saturated compounds of Table III because the former are more active in the indicated assays. Thus, without the teachings of the present application there would be no motivation of a skilled artisan to modify the compounds disclosed in the Jones reference to meet the limitations of the instant claims.

Even if there were motivation to combine, there would not be a reasonable expectation of success. In an effort to support such an expectation, Examiner alleges that all of the compounds in the Jones reference (or at least those in Table III) have similar properties. Office Action, page 3. Applicant disagrees. Specifically, there is at least a 50-fold range in the efficacy of the Table III compounds in the "reversal of reserpine-induced hypothermia" assay and a difference of 16% in the "% inhibition of 2-HT uptake" assay. Thus, because the data provided in Table III shows that variations in the structure of the compounds significantly affects the properties of the compounds with respect to their performance in the indicated assays, one of ordinary skill in the

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art would not have a reasonable basis to accurately predict whether any particular modification would result in a beneficial effect, a negative effect or no effect at all on the biological activity of the compound. Thus, one would not be motivated to modify the Jones reference compounds to obtain a useful anti-depressant as any such modification would not be predictable.

Further, the Jones reference teaches that the only disclosed compounds which meet or exceed the activities of known antidepressants (*i.e.* compounds 5, 6, 15, 16, 17 and 18) all belong to the olefinic series of Table I. Page 161, right column, last full paragraph; and page 162, Table I. Thus because the saturated compounds of Table III are less active in the indicated assays than known antidepressants, a skilled artisan would expect modified versions of the Table III compounds to be less successful as antidepressants. Therefore, since the present claims are directed to saturated compounds corresponding to the generic structure of Table III there would be no reasonable expectation based on teachings of Jones that such compounds would be successful antidepressants.

Applicant respectfully submits that a reference must only be used for what it fairly teaches. Hindsight provided by the application cannot be used to provide the missing motivation or expectation of success. The Jones reference does not disclose compounds that meet the required limitations of the instant claims, it does not provide any motivation for a skilled artisans to modify the compounds shown in the reference, and there is no teaching that would suggest that modifications to the compounds would have a reasonable expectation to succeed in the claimed method. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

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Conclusion

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

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